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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/284,107	10/25/1999	TON LOGTENBERG	313632000600	1900

7590 05/20/2002

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EXAMINER	
BHATTI, TAHIRA H	
ART UNIT	PAPER NUMBER
1627	

DATE MAILED: 05/20/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/284,107	LOGTENBERG ET AL.	
	Examiner	Art Unit	
	Tahira H Bhatti	1627	

-- Th MAILING DATE of this communication appears on the cov r sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 March 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *2,4 and 11-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3 and 5-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Response to Amendment

1. Applicant's amendment dated 3/12/02 in paper no. 20 is acknowledged.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Status of the Claims

2. New claims 13-18 are added by applicant's amendment dated 3/12/02 in paper no. 20 is acknowledged

3. Claims 1-18 are currently pending.

4 Claims 2,4, 11-18 are withdrawn from consideration as being directed to a nonelected invention.

5. Claims 1,3 and 5-10 are under consideration

Withdrawn Objection(s) and/or Rejection(s)

6. Applicant's amendment has overcome the indefinite rejection of former claim 1, 3 and 7 as of the previous office action (e.g. directed to a relative term, "specific binding," "comprising" and "encoding").

7. Applicant's objection has overcome the anticipation and obviousness rejections over the Kettleborough et al Pat. N0. 58/44093.

Outstanding Objection(s) and/or Rejection(s)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

8. The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms

as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claim 1 (and dependent claims) is rejected under 35 U.S.C. 112 first and second paragraph since there is no metes and bounds regarding which peptides capable of binding and peptides not capable of binding , nor the relative information of synthesizing oligopeptides derived from the proteinaceous target within the scope of the presently claimed invention is provided.

10. Applicant's arguments as they apply to claims 1,3 and 5-10 regarding enablement and indefiniteness were considered but deemed nonpersuasive for the following reasons. Applicant first argues that "why should claim 3 provide the metes and bounds as to which peptide binds and which do not, is based on a misapprehension of the claimed invention", Moreover the applicant asserts that, "in the instant application evidence is provided that no information concerning the specific structure of the binding peptide is necessary to identify a peptide that binds a particular oligonucleotide." This argument is non-persuasive. It cannot be apprehended as to, how an unknown peptide or antibody bind to an unknown proteinacious target, and drive unknown binding peptides and unknown non-binding peptides from the unknown proteinacious target. The peptides that bind and those that do not bind are derived from a proteinacious target. In addition applicant has failed to define the encoding sequence in claim 7. Accordingly the above rejection is maintained.

11. Claims 1, 5-7, 10 is rejected under 35 U.S.A. 102(b) as being clearly anticipated by Ladner, W0 9,215,677

12. Ladner clearly shows that the genes encoding disulfide _bonded micro-proteins (i.e. peptides) are expressed on the surfaces of bacterial cells, spores or phage. The resulting display phage library in his study includes BPT1 (58 residues) and Crambin (46) residues are screened for members having the ability to bind to a proteinaceous target of interest. The phage display library (peptides or antibodies) are within the scope of the presently claimed (e.g. claims 1 and 3) inventions.

Discussion

13. Applicant arguments directed to the above rejection was considered but deemed nonpersuasive for the following reasons. Applicant argues that the reference completely fails to disclose the synthesis of oligopeptides on a solid phase. However, the reference clearly discloses applicant's method steps. Ladner discloses that the genes encoding disulfide-bonded micro-proteins (i.e. peptides) are expressed on the surfaces of bacterial cells, spores or phage,having the ability to bind to a proteinaceous target of interest. And further on page 6 lines 34-35 discloses that peptides are synthesized on solid supports. Accordingly the '677 reference clearly teaches solid-support bound "oligopeptides **derived from** a protein target" within the scope of the present broad claim(s) limitation. The reference further teaches that membranes are utilized for the synthesis of peptides. In addition applicant has failed to

provide specifically what solid supports are intented for the synthesis of peptides. Accordingly the above rejection is maintained.

14. Claim 1 and 3 are rejected under 35 U.S.A. 102(b) as being clearly anticipated by Mehta et al, W0 92/087,38 or its U.S. equivalent example of Ishikawa; U.S. Pat. N0 5,236,849.

15. The cited reference discloses a test sample containing Hepatitis C Virus (HCV) antigen, contacting with a solid phase to which a monoclonal or polycolonal anti-HCV antibody or a fragment has been bound. Here it is clearly understood that Mehta et. al., described a solid phase with specific proteins or antigens, for binding specific antibodies that are within the scope of the presently claimed (e.g. claims 1 and 3) inventions.

DISCUSSION

16. Applicant arguments directed to the above rejection was considered but deemed nonpersuasive for the following reasons. Applicant argues that the above reference fails to disclose the use of a display package or the synthesis of oligopeptides on a solid phase, derived from the proteinaceous target. This argument is not persuasive. The Mehta et al reference discloses that, monoclonal antibodies recognize (specifically binds) specific epitope, of full-length proteins. Page 17 lines 20-30. The reference further discloses on page 18 lines 24-25, that peptides are assembled on a resin support by solid phase synthesis. See the entire document specially, page 17, lines 5-17. Accordingly the '738 reference clearly teaches solid-support bound

"oligopeptides **derived from** a protein target" within the scope of the present broad claim(s) limitation. Both references i.e. '738 in view of '848 teach every element of the claims. Accordingly the above rejection is maintained.

17. Claims 1 and 3 are rejected under 35 U.S.C. 102 (b) and 35 U.S.C. 103(a) as being unpatentable over WO. Patent No. 95/159,82 to Barsomian.

18. The reference teaches the use of a replicable genetic display package in an immunoreactive context which permits the antibody (e.g. peptide/protein) to bind to an antigen (protein), that is contacted with the display package, which embraces applicants claimed inventions, see the entire document, especially lines 26-31 and 32-37 on page 2. Further more it discloses that the display library can be a phage and can be generated on a bacterial cell surface or a spore see lines 1-3 page 3.

Discussion

19. Applicants arguments directed to the above rejection was considered but deemed nonpersuasive for the following reasons. Applicants argues that the reference differs from the claimed invention in that it fails to disclose the synthesis of oligopeptides on a solid phase, derived from a proteinaceous target and the use thereof to contact peptides displayed on a replicable display package. The applicant further argues that no suggestion or motivation has been provided as to why it would have been obvious at the time of the invention for one of ordinary skill in the art to modify Barsomian et al. to include the synthesis of oligopeptides. This argument was not persuasive. The '982 reference, lines 30-32 page 29 teaches, that the display package is contacted with the

target antigen and that antibodies of the display package that are able to specifically bind the antigen are isolated, line 36 page 29, and lines 1-3 page 30. The reference further teaches, that the target antigen is immobilized on an insoluble carrier, and that binding of antibody to a target antigen can be fractioned from those of any non-specific binding of antibodies to the target antigen, (referes to claim 3). Accordingly the '982 reference clearly teaches solid-support bound "oligopeptides **derived from** a protein target" within the scope of the present broad claim(s) limitation and additionally, the reference clearly suggests the claimed invention, and those skilled in the art would be motivated to modify the Barsomian et al. reference because of the motivation to generate a powerful method for rapidly selecting antibodies with the desired specificities and include a further step to synthesize an oligopeptide on a solid phase derived from the target antigen (proteinnaceous target, Claim 1), and further contact the antibodies with the oligopeptide, and isolate the specifically binding, from those of any non-specific binding of antibodies to the oligopeptides. Accordingly the above rejection is maintained.

New Grounds of Rejections(s)

20. Claims 1, 3 and 5-10 are rejected under 35 U.S.C. 102 (b) as being unpatentable over Kruif et al J. Mol. Biol. 248:97-105, 1995.

Kruif et al disclose construction of ScFv libraries expressed on the surface of filamentous phage (replicable display package) and binding of the said ScFv fragment (peptide) to antigens. The reference further discloses that specific monoclonal phage

antibodies (MoPhabs) i.e. peptides were isolated, when the A2 fragment (oligopeptide derived from proteinacious target) of a complete protein (proteinacious target) was used for selection. The reference also teaches that, the A2 fragment is less accessible to phage antibody (Phabs), when the whole protein is used for selection and that additional specificities can be obtained by using portions of a molecule (oligopeptides) for selection. Page 102 col.1, second paragraph. The reference further teaches that scFv fragments bind to antigens which are synthesized on solid-phase, page 102, col. 1 lines 6-8. The use of optimal binding peptides (e.g. epitopes) for therapeutic use (e.g. vaccine) is also taught. Accordingly, the Kruif et al reference suggests the synthesizing of one or more oligopeptide "derived from a protein target" on a substrate for screening a phage library peptide ligand.

21. Claims 1,3 and 5-10 are rejected under 35 U.S.C. 103(a) as obvious over Kruif et al in view of Van Oirschot et al WO 91/049,86, (1991) and /or Geysen WO 84/035,64

Kruif et al disclose construction of ScFv libraries expressed on the surface of filamentous phage (replicable display package) and binding of the said ScFv fragment (peptide) to antigens. The reference further discloses that specific monoclonal phage antibodies (MoPhabs) i.e. peptides were isolated, when the A2 fragment (oligopeptide derived from proteinacious target) of a complete protein (proteinacious target) was used for selection. The reference also teaches that, the A2 fragment is less accessible to phage antibody (Phabs), when the whole protein is used for selection and that

additional specificities can be obtained by using portions of a molecule (oligopeptides) for selection. Page 102 col.1, second paragraph. The reference further teaches that scFv fragments bind to antigens which are synthesized on solid-phase, page 102, col. 1 lines 6-8. The use of optimal binding peptides (e.g. epitopes) for therapeutic use (e.g. vaccine) is also taught. Accordingly, the Kruif et al reference suggests the synthesizing of one or more oligopeptide "derived from a protein target" on a substrate for screening a phage library peptide ligand.

22. Kruif et al differ from the presently claimed invention (if at all) since, although Kruif et al suggests, it nevertheless fails to specifically disclose, making a plurality of oligopeptide fragments of a target protein for phage library screening.

23. The making of oligopeptide fragments of target proteins for screening with corresponding binding ligands (e.g. antibodies) utilizing conventional oligopeptide synthetic and screening protocols is known in the art.

24. For example, the '986 reference teaches oligopeptides derived from glycoprotein 1 (g 1) to produce monoclonal antibodies using the PEPSCAN method. The reference further teaches that these oligopeptide that are reactive with antibodies against glycoprotein 1, are those oligopeptide fragments that have a specific reactivity with antibodies against g1, page 6 lines 10-16. The oligopeptide are synthesized, and are arranged on a nitrocellulose strip and by successively washing and adding a labeled antibody the specific reaction (binding) is determined, page 9, lines 31-33

25 Additionally or alternatively Geysen teaches a method of detecting a sequence of amino acids (peptide) that is antigenically active within a known amino acid sequence of a protein (proteinacious target), and contacting each of said peptides with antibody against the protein. The '564 reference further teaches that each sequence determined is then synthesized. The peptide synthesized is then attached to a suitable solid support See abstract and pages 5-6.

26. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the Kruif et al reference teaching in order to obtain oligopeptides derived (e.g. epitopes) from target proteins (utilizing conventional synthetic protocol as exemplified in the '986 reference or Geysen) and screen the oligopeptides using its corresponding ligand (e.g. antibody) in conventional screening assays in order to determine optimal binding oligopeptide compounds (e.g. epitopes) as suggested in the Kruif reference (e.g. for therapeutic use such as in a vaccine).

General information regarding further correspondence

27. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Tahira Bhatti whose telephone number is (703) 605-1203.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jyothsana Venkat (art unit 1627), can be reached at

(703) 308 0570

Any inquiry of a general nature, or relating to the status of this application, should be directed to the Group receptionist whose telephone number is (702) 308-0196

Tahira Bhatti (art unit 1627)

May 17, 2002

BENNETT CELSA
PRIMARY EXAMINER